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Letter to the Editor

Neurological Complications in Pediatric Patients after SARS-CoV-2 Infection

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Letter to the Editor

We read with interest the article by Roux *et al*. on a retrospective, multicenter study of the type, severity, and long-term consequences of neurological manifestations in children hospitalized between January 2000 and March 2022 due to SARS-CoV-2 infection (SC2I) [1]. The most common neurological manifestations were encephalitis and meningoencephalitis (32%), cerebral imaging results were abnormal in 68%, half of the children had to be admitted to the pediatric intensive care unit (PICU), and one-third had cognitive deficits at follow-up [1]. Abnormal cerebral imaging results were associated with an increased risk of admission to the PICU and neurological complications at discharge [1]. The study is noteworthy, but some points should be discussed.

The first point relates to the retrospective design of the study [1]. Retrospective designs have several disadvantages [2]. A retrospective design allows only limited control over the sample population and only limited control over the type and quality of predictor variables. In addition, the relevant predictors may not have been recorded in the medical records, and it may be difficult or impossible to identify confounding variables and causalities. It is also inevitable that some information will be missing, as the data is based on the review of medical records that were not originally intended for collection. Selection and recall errors further influence the results [2].

The second point is the discrepancy between the objectives stated in the summary ("included due to SC2I") and the section on methodology in the summary ("included due to neurological complications of SC2I") [1]. This should be clarified. If only patients with neurological complications were included, it is difficult to calculate figures for the frequency of neurological complications in this cohort. In this case, it should also be stated who diagnosed the neurological complications prior to inclusion.

The third point is that SARS-CoV-2 vaccines were already available in 2021 and 2022, but it was not reported how many of the 71 patients included were vaccinated and how many were not [1]. Knowing the vaccination status is crucial because SARS-CoV-2 vaccination (SC2V) can not only prevent a milder or even SC2I, but also prevent neurological sequelae. Did the vaccinated patients have less severe neurological complications than the unvaccinated patients?

The fourth point is that SC2I was partly diagnosed using antigen tests [1]. Since the specificity and sensitivity of antigen tests is lower than that of PCR tests [3], it is conceivable that at least some of the patients did not actually have SC2I, but another infection. We should know how many of the included patients had SC2I based on an antigen test.

The fifth point is that the neurological outcome was not assessed in all patients within the same period after discharge, which makes it difficult to draw conclusions about the frequency of neurological complications at follow-up. The longer the period between discharge and follow-up, the more likely it is that patients will not show any neurological impairments.

The sixth point is that, according to Table 1, 25 of the 71 patients included had neurological comorbidities such as epilepsy, febrile seizures, psychomotor retardation, or learning difficulties [1]. How was it ensured that a seizure in a patient with SC2I-associated encephalitis was due to the acute infection and not to a previously diagnosed epilepsy? To rule out bias in this regard, it would have been useful to exclude all patients with neurological comorbidities from the analysis.

In summary, this study has limitations that qualify the results and their interpretation. Eliminating these limitations could make the conclusions more compelling and strengthen the study's message. All open questions must be clarified before readers can uncritically accept the conclusions of the study. To assess the type, frequency, and outcome of neurological complications in pediatric patients with SC2I, a prospective design would be desirable and patients with previous neurological comorbidities should have been ruled out.

Declarations

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